RESEARCH ARTICLE

The Effectiveness of Intravenous Magnesium Sulfate for Deliberate Hypotension in Rhinoplasty

Seyed Mohammad Mireskandari[1], Kasra Karvandian[1]*, Afshin Jafarzadeh[1], Jalil Makarem[1], Shahram Samadi[1], Asghar Hajipour[1], Negar Eftekhar[1], Sanaz Shabani[1], Mohammad Fatehi[1], Jayran Zebardast[2]

Background: Deliberate hypotension is a strategy that reduces intraoperative bleeding and increases the speed of surgery in otolaryngology procedures. Magnesium (Mg) sulfate is a vasodilator agent that reduces intraoperative hypnotic requirements and in combination with analgesic agents, it reduces intraoperative and postoperative pain. In this study we evaluated the use of intravenous Mg sulfate for inducing deliberate hypotension in rhinoplasty.

Methods: Sixty ASA I, II patients aged between 18 to 45, scheduled for rhinoplasty were recruited into a randomized clinical trial. Patients were randomly assigned into placebo (group P) and Mg sulfate (group M) groups. For patients in group M, 40m/kg Mg sulfate was administered before induction and continued with 15mg/kg/hr infusion during the operation. Patients of group P received normal saline as placebo. In each group mean arterial pressure (MAP), mean heart rate, amount of bleeding, anesthetic agents, opioid requirement and duration of surgery were recorded. The incidence of nausea, vomiting, shivering and the score of pain were recorded in post-operative period in both groups.

Results: Patients in group M had lower MAP (P= 0.0001), less intraoperative bleeding (P=0.0001), lower anesthetic agents (P=0.0001) and opioid consumption (P=0.001), and shorter duration of procedure (P=0.0001). Mean heart rate was lower in group P (P=0.001). Moreover, surgeon`s satisfaction was more in group P (P=0.001).They also had less incidence of post-operative nausea and vomiting (P=0.008), shivering (P=0.001) and lower pain scores postoperatively (P=0.0001).

Conclusion: Magnesium sulfate can be a useful drug to induce controlled hypotension in rhinoplasty surgery. By employing this agent patients have better anesthetic condition and recovery profile.

Keywords: magnesium sulfate; controlled hypotension; rhinoplasty

Hypotensive anesthesia is a strategy for reducing bleeding during surgical procedures and providing a perfect operative field in special conditions like head and neck surgeries [1-2]. By employing deliberate hypotension, the speed of surgery will improve because the surgeon has better view of operation field [3-5]. Nowadays there are many anesthetic techniques suggested to reduce mean arterial pressure (MAP) during operation by using various anesthetic agents or adjuvant drugs [3-6]. Magnesium (Mg) sulfate is a vasodilator agent which has a number of applications in anesthesia [7-14]. Mg sulfate reduces intraoperative hypnotic requirements and in combination with analgesic agents, it reduces intraoperative and postoperative pain [12-16], so in this study we aimed to evaluate the use of intravenous Mg sulfate for inducing controlled hypotension in rhinoplasty.

Methods

After obtaining institutional ethics committee and patients informed consent, sixty ASA I, II patients aged between 18 to 45, scheduled for rhinoplasty in our general hospital between March 2014 and March 2015, were recruited into a randomized triple blinded clinical trial. Patient with any history of underlying disease, obesity with body mass index greater than 30 and any history of drug abuse were excluded from the study. The study cases were randomly assigned into two groups by using computer random-generated code numbers which had been placed in opaque, sealed envelopes by a person not involved in the study. Patients were administered 40 mg/kg of solution of Mg sulfate 10% (group M, n=30) and normal saline as a placebo (group P, n=30), which were prepared in 500 ml normal saline bottles got ready by an expert anesthetic nurse and encoded by a secretary before induction of anesthesia. They also received 15mg/kg/hour infusion of the same prepared solution during the operation. The study was triple blinded because neither the patient, nor the surgeon and nor the anesthesiologist who anesthetized the patient were informed about the content of solutions to each patient were administered After premedication with midazolam (0/.02 µg/kg) and fentanyl

From the [1]Department of Anesthesiology and Critical Care, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.
[2]Msn student of electronic learning in medical education, virtual school, Tehran University of Medical Sciences, Tehran, Iran.
Received: 1 September 2015, Revised: 23 September 2015, Accepted: 8 October 2015
The authors declare no conflicts of interest.
*Corresponding author: Kasra Karvandian, MD, Department of Anesthesiology & Critical Care. Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran. E-mail: k.karvandian@gmail.com

(2µg/kg), induction of anesthesia was performed by propofol (2mg/kg), and atracurium (0.6 mg/kg) in all patients and then proper size of cuffed endotracheal tube applied for each patient in both groups. Infiltration of 2% lidocaine and 1:100.000 epinephrine was administered 10 min before surgery by the surgeon in all patients. The anesthesia was maintained by 50% N2O and 0.8- 1.5% isoflurane, to achieve target mean arterial pressure (MAP). During the operation infusion of remifentanil (0.1-0.2µg/kg) was administered with either Mg sulfate 10% (15mg/kg/hour) or equal volume of normal saline as placebo in both groups. All patients were in 30 degree head up position during the procedure and monitored by electrocardiography, pulse oximetery, capnography and non invasive blood pressure measuring. The goal of intraoperative blood pressure was to maintain MAP between 55 to 75 mmHg, and if the patient developed with higher MAP, first the administered dose of isoflurane was increased to maximum 1.5% and then the infusion rate of remifentanil was increased up to maximum dose of 0.2µg//kg. Ephedrine was considered as vasopressor agent for MAP< 50 and atropine was considered as vagolytic agent for heart rate <60. Hemodynamic variables were recorded every 5 minute and total dose of remifentanil was recorded for each patient. All surgeries were performed by two surgeons.

For estimation of the amount of bleeding in the surgical field, all the sterile gauze sponges in surgical set were weighed [2] by a KIA SCALE model BL 1000 with accuracy of 0.01 gr and after the operation, they were weighed once more and the difference in gram scale was calculated as 1.03 gr for each ml blood. The amount of blood in the suction was added to the result.

The incidence of post-operative nausea and vomiting and shivering in the post anesthesia care unit (PACU) was recorded. We also rated postoperative pain in PACU by employing PAULA the PAIN-METER [17].

At the end of each procedure, duration of surgery was recorded and the surgeon was asked about his satisfaction with the operative conditions.

With the help of SPSS version 16 (SPSS Inc., Chicago, IL, USA), the data were analyzed by Mann-Whitney test, analysis of variance, and student t-test. P value ≤ 0.05 was considered significant.

Results

Two groups were similar with respect to demographic characteristics and showed no statistically significant difference. Also operative time and baseline vital signs did not differ among the groups (Table1).

The average MAP was 57.50 ±1.7 in group M and 73.26 ±1.50 in group P, which was statistically significant different between two study groups (P=0.0001). Moreover, mean heart rate was 70. 56 ±1.81 in group M and 65.56±1.6 in group P, which showed statistically significant difference (P= 0.001). The amount of intraoperative bleeding was statistically less in group M compared with group P (228.66± 30.16 ml and 393.06±13.51ml respectively, P= 0.0001). Surgeons were satisfied with the surgical conditions in 28/30 cases (63.6%) in group M and 16/30 cases in group P (36.4%), which showed more satisfaction regarding surgical field in group M (P= 0.001). Meanwhile, operation time was statistically different in patient of group M compared to patients in group P (87.46±14.29 minutes versus 122.9± 19.30 minutes, P= 0.0001). Anesthesia team administered less anesthesia drugs in group M compared to group P (Table 1). Patients in group M had lower incidence of nausea and vomiting and shivering compared to patients in group P postoperatively (Table 1). Ephedrine was used for one patient (3.3%) in group M and 4 patients (13.3%) in group P (P=0.161). In addition atropine was used for 2 patients (6.7%) in group M and 4 patients (13.3%) in group P (P=0.389). Patients of group M had less pain compared to patients in group P which was statistically significant (P= 0.0001).

Discussion

Ear, nose and throat procedures, are prone to significant amount of bleeding due to hyper vascular areas of surgical field, so deliberate hypotension is necessary to improve the quality of surgical condition [2,18-19]. There are many anesthetic techniques which employ either anesthetic drugs with vasodilatory effects or some adjuvant antihypertensive agents to reduce MAP during operation [3-6]. Mg sulfate is a vasodilator agent which has a number of applications in anesthesia for many years [7-14].

In this study our aim was to evaluate the use of intravenous Mg sulfate for inducing deliberate hypotension in rhinoplasty. Deliberate hypotension is reduction of MAP to 50-65 mmHg or a 30% reduction of baseline MAP [1,3]. In this study the aim of MAP was between 55-75 mmHg which provided optimal surgical situation. In operations with deliberate hypotension, patients bleed less and they need fewer blood transfusions [20-21].

In this trial, we recorded lower average MAP in group M, and those patients who received Mg sulfate had lesser amount of intraoperative bleeding. The time of operation was less in this group, because the surgeon had better view of operation field and time consumption for suctioning blood and drying the surgical field was less [3-5]. Mechanism of vasodilation by Mg sulfate is first by inhibition release of calcium in smooth muscles and then by release of nitric oxide from endothelial cells, so it can directly reduce vascular tonicity [7]. Calcium is a key ion component in release of catecholamines in response to sympathetic stimulation and magnesium inhibits calcium influx by blocking calcium ion channels [8-9]. This competition leads in blocking the release of catecholamines and adrenergic responses in sympathetic stimulation due to pain of surgery or any other causes [8-10]. There are also evidences in animal studies that magnesium blocks the release of catecholamines and vasopressin in spontaneous hypertension [11] and it is one of the important agents in therapeutic regimens of hypertensive crises in preeclampsia [8]. Also this drug is useful in tetanus and pheochromocytoma, which are situations of excess catecholamine release [8,16]. There are some studies that showed beneficial effects of using Mg sulfate in aortic cross clamp situations to improve renal perfusion by its vasodilatory effects [15].

Mg sulfate reduces intra operative hypnotic requirements and in combination with analgesic agents, it poseses some antinociceptive activity [12-15], as we observed less volatile anesthetic consumption in group M and the target MAP was achieved with less remifentanil consumption. Patients in group P had lower mean heart rate, which might be due to higher remifentanil doses in this group. We also recorded fewer incidences of post-operative nausea and vomiting,

Table 1- The demographic and outcome variables in study groups

Variables	Mg sulfate group	Placebo group	p-value
Age (y)	27.9±0.4	27.97±0.18	0.4
Female (%)/Male (%)	12(40%)/18(60%)	11(36.7%)/19(63.7%)	0.7
MAP (mmHg)	57.5 ±1.737	73.26±1.507	0.0001
HR	70.56±1.8	65.56±1.63	0.001
bleeding (ml)	233.66±30.16	363.06±13.513	0.0001
Remifentanil (µg)(	233.66±30.16	363.06±13.513	0.0001
Isoflurane dose (%)	0.870±0. 80	1.20±0.12	0.001
Operation time (min)	87.46±14.29	129.9±19.30	0.0001
Anesthesia time (min)	105.53±11.13	148.81±12.47	0.0001
Pain score	4.03±.88	8.10±1.09	0.0001
Ephedrine used	1(3.3%)	4(13.3%)	0.161
Atropine used	2(6.7%)	4(13.3%)	0.389
Surgeon Satisfaction	28(93.3%)	16(53.3%)	0.001
Vomiting	13(43.3%)	23(76.7%)	0.0001
Shivering	10(33.3%)	23(76.7%)	0.0001

*Data are expressed as Mean ±sd

which may be the result of less opioid and volatile anesthetic consumption in group M intraoperatively [22-23].

One of the applications of Mg sulfate is to treat post-operative shivering [24], in this clinical trial, we had significant less incidence of shivering in group M, and this may be the result of prophylactic effect of Mg sulfate for shivering [25-27].

In this study we also recorded lesser pain scales in PACU in patients of Mg sulfate group which may confirm the preemptive effect of Mg sulfate [28] or it may be the result of the hyperalgesia caused by infusion of higher doses of remifentanil in control group [29-31].

Unfortunately, we did neither measure serum concentration of Mg intraoperatively nor postoperatively. But none of the patients who received Mg sulfate showed any evidence of clinically significant residual neuromuscular block in the PACU which probably is the result of administration of just a single intubating dose of muscle relaxant at the beginning of anesthesia process and not repeating any additional dose of muscle relaxant during the remaining anesthesia time until the end of surgery.

Conclusion

As conclusion we found that Mg sulfate as a useful agent for controlled hypotension in rhinoplasty, because by administering this agent to the patients, they bleed less, the operation time was reduced, and besides greater surgeon`s satisfaction and several other advantages as discussed earlier.

References

1. Boonmak S, Boonmak P, Laopaiboon M. Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS). Cochrane Database Syst Rev. 2013; 6: CD006623.
2. Na Young K, Young-Chul Y, Duk-Hee C, HyeMi L, Young-Soo J, Sun-Joon B. The effects of oral atenolol or enalapril premedication on blood loss and hypotensive anesthesia in orthognathic surgery. Yonsei Med J. 2015; 56(4): 1114–1121.
3. Degoute CS. Controlled hypotension: a guide to drug choice. Drugs. 2007; 67(7):1053-76.
4. Prasant MC, Kar S, Rastogi S, Hada P, Ali FM, Mudhol A. Comparative study of blood loss, quality of surgical field and duration of surgery in maxillofacial cases with and without hypotensive anesthesia. J Int Oral Health. 2014; 6(6):18-21.
5. Tagarakis GL, Whitlock RP, Gutsche JT, Diegeler A, Patel PA, Daskalopoulos ME, et al. New frontiers in aortic therapy: focus on deliberate hypotension during thoracic aortic endovascular interventions. J Cardiothoracic Vasc Anesth. 2014; 28(3):843-7.
6. Spielberg DR, Barrett JS, Hammer GB, Drover DR, Reece T, Cohane CA, et al. Predictors of arterial blood pressure control during deliberate hypotension with sodium nitroprusside in children. Anesth Analg. 2014; 119(4):867-74.
7. Goldman RD, Mounstephen W, Kirby-Allen M, Friedman JN. Intravenous magnesium sulfate for vaso-occlusive episodes in sickle cell disease. Pediatrics. 2013; 132(6):e1634-41.
8. Honarmand A, Safavi M, Badiei S, Daftari-Fard N. Different doses of intravenous Magnesium sulfate on cardiovascular changes following the laryngoscopy and tracheal intubation: A double-blind randomized controlled trial. J Res Pharm Pract. 2015; 4(2):79-84.
9. Komaki F, Akiyama T, Yamazaki T, Kitagawa H, Nosaka S, Shirai M. Effects of intravenous magnesium infusion on in vivo release of acetylcholine and catecholamine in rat adrenal medulla. Auton Neurosci. 2013; 177(2):123-8.
10. Kalra NK, Verma A, Agarwal A, Pandey H. Comparative study of intravenously administered clonidine and magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol. 2011; 27(3):344-8.
11. Laurant P, Touyz RM, Schiffrin EL. Effect of magnesium on vascular tone and reactivity in pressurized mesenteric resistance arteries from spontaneously hypertensive rats. Can J Physiol Pharmacol. 1997; 75(4):293-300.
12. Telci L, Esen F, Akcora D, Erden T, Canbolat AT, Akpir K. Evaluation of effects of magnesium sulfate in reducing intraoperative anaesthetic requirements. Br J Anaesth. 2002; 89:594-8.
13. Kroin JS, McCarthy RJ, Von Roenn N, Schwab B, Tuman KJ, Ivankovich AD. Magnesium sulfate potentiates morphine antinociception at the spinal level. AnesthAnalg. 2000; 90(4):913-7.
14. Choi JC, Yoon KB, Um DJ, Kim C, Kim JS, Lee SG. Intravenous magnesium sulfate administration reduces propofol infusion requirements during maintenance of propofol-N2O anesthesia: part I: comparing propofol requirements according to hemodynamic responses: part II: comparing bispectral index in control and

magnesium groups. Anesthesiology. 2002; 97(5):1137-41.
15. Jang Y, Shin HY, Kim JM, Lee MY, Keum DY. Effects of magnesium sulfate on supraceliac aortic unclamping in experimental dogs. J Korean Med Sci. 2005; 20(4):612-7.
16. Sanath Kumar SB, Date R, Woodhouse N, El-Shafie O, Nollain K. Successful management of phaeochromocytoma using preoperative oral labetalol and intraoperative magnesium sulfate: report of four cases. Sultan Qaboos Univ Med J. 2014; 14(2):e236-40.
17. Machata AM, Kabon B, Willschke H, Fässler K, Gustorff B, Marhofer P, et al. A new instrument for pain assessment in the immediate postoperative period. Anaesthesia. 2009; 64(4):392-8.
18. Hadavi MR, Zarei Y, Tarogh S. Comparison of effects of labetalol and nitroglycerine on intraoperative blood loss and surgical field quality in rhinoplasty surgery. World J Plast Surg. 2015; 4(1):60-5.
19. Gruber RP, Zeidler KR, Berkowitz RL. Desmopressin as a hemostatic agent to provide a dry intraoperative field in rhinoplasty. Plast Reconstr Surg. 2015; 135(5):1337-40.
20. Choi WS, Samman N. Risks and benefits of deliberate hypotension in anaesthesia: a systematic review. Int J Oral Maxillofac Surg. 2008; 37(8):687-703.
21. Paul JE, Ling E, Lalonde C, Thabane L. Deliberate hypotension in orthopedic surgery reduces blood loss and transfusion requirements: a meta-analysis of randomized controlled trials. Can J Anaesth. 2007; 54(10):799-810.
22. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, Kadioglu H, et al. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Braz J Anesthesiol. 2015; 65(3):191-9.
23. Öbrink E, Jildenstål P, Oddby E, Jakobsson JG. Post-operative nausea and vomiting: update on predicting the probability and ways to minimize its occurrence, with focus on ambulatory surgery. Int J Surg. 2015; 15:100-6.
24. Wadhwa A, Sengupta P, Durrani J, Akça O, Lenhardt R, Sessler DI, et al. Magnesium sulfate only slightly reduces the shivering threshold in humans. Br J Anaesth. 2005; 94(6):756-62.
25. Faiz SH, Rahimzadeh P, Imani F, Bakhtiari A. Intrathecal injection of magnesium sulfate: shivering prevention during cesarean section: a randomized, double-blinded, controlled study. Korean J Anesthesiol. 2013; 65(4):293-8.
26. Gozdemir M, Usta B, Demircioglu RI, Muslu B, Sert H, Karatas OF. Magnesium sulfate infusion prevents shivering during transurethral prostatectomy with spinal anesthesia: a randomized, double-blinded, controlled study. J Clin Anesth. 2010; 22(3):184-9.
27. Manouchehrian N, Mohammadian A, Sanie MS, Faridi-Tazeh-kand N, Sanatkar M. A comparison of the therapeutic effect of tramadol and meperidine for treatment of shivering after spinal anesthesia in elective caesarean section. Archives of Anesthesiology and Critical Care. 2015; 1(2): 50-54.
28. Ryu JH, Sohn IS, Do SH. Controlled hypotension for middle ear surgery: a comparison between remifentanil and magnesium sulfate. Br J Anaesth. 2009; 103(4):490-5.
29. Rezae M, Naghibi K, Taefnia AM. Effect of pre-emptive magnesium sulfate infusion on the post-operative pain relief after elective cesarean section. Adv Biomed Res. 2014; 3:164.
30. Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. Br J Anaesth. 2014; 112(6):991-1004.
31. Chen Y, Yao Y, Wu Y, Dai D, Zhao Q, Qiu L. Transcutaneous electric acupoint stimulation alleviates remifentanil-induced hyperalgesia in patients undergoing thyroidectomy: a randomized controlled trial. Int J ClinExp Med. 2015; 8(4):5781-7.